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10/055,713	01/22/2002	Andrew Jamieson	8325-0026	6239

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EXAMINER

COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/055,713

Applicant(s)

JAMIESON ET AL.

Examiner

Cynthia Collins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-11, 14, 17-19 and 21-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-11, 14, 17-19 and 21-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0605.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 10, 2004 has been entered.

Claims 5, 12-13, 15-16 and 20 are cancelled.

Claims 1, 6-7, 9-11 and 14 are currently amended.

Claims 21-33 are newly added.

Claims 1-4, 6-11, 14, 17-19 and 21-33 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Election/Restrictions

Applicant's election with traverse of Group IX, drawn to a composition comprising or encoding a modified zinc finger protein and a C1 functional domain in the reply filed on June 13, 2005 is acknowledged.

The traversal is on the ground(s) that the inventions must be independent or distinct as claimed. Applicant points out that the specific protein functional domains appear only in dependent claims 14 and 33, and maintains that no reasons are given with

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regard to independence or distinctness of independent claims 1 and 21. Applicant also maintains that the Office acknowledges that the independent claims (claims 1 and 21) are not patentably distinct from each other, as they are classified in the same class and subclass.

This is not found persuasive because dependent claims may be restricted when they are directed to independent or distinct inventions. This is also not found persuasive because, as set forth at page 6 of the office action mailed May 10, 2005, the specific protein functional domains (p300, CBP, PCAF, SRC1, PvALF, ERF-2, OsGAI, HALF-1, C1, AP1, ARF-5, ARF-6, ARF-7, ARF-8, CPRF1, CPRF4, MYC-RP/GP and TRAB1) are distinct because they originate from different species of organisms and because they differ both structurally and functionally. This is additionally not found persuasive the classification of claims in the same class and subclass does not suggest that the subject matter of the claims is not patentably distinct, as every class and subclass contains numerous different inventions that are patentably distinct from each other.

The traversal is also on the ground(s) that a search of the restricted groups would not pose a serious burden. Applicant points out that any search for references relevant to the subject matter of independent claims 1 and 21 (classified in all 18 Groups) will necessarily and in all cases reveal art relevant to all claims, including modified plant zinc finger proteins comprising the various functional domains recited dependent claims 14 and 33. Applicant maintains that there is no need to search for references relevant to the various functional domains, as they are not claimed independently of their association with a modified plant ZFP.

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This is not found persuasive because references relevant to the various functional domains must be searched separately from their association with a modified plant ZFP even though they are not claimed independently. A proper search is not limited to the subject matter of the independent claims, as relevant art not identified in a search of the independent claims, such as art useful under 35 USC 103, may exist.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

Claims 1-4, 6-11, 14, 17-19 remain rejected, and claims 21-33 are rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.

Applicant's arguments filed June 10, 2004, have been fully considered but they are not persuasive.

Applicant maintains that the pending claims are directed to molecules clearly described in the specification as filed. Applicant points out that the claims have been amended to make explicit that the claimed modified plant zinc finger proteins necessarily have a different amino acid sequence than naturally occurring plant zinc finger proteins, either because the inter-finger spacing is shortened (claim 1 and claims dependent therefrom) and/or because the amino acid sequence of the recognition region is altered as compared to a naturally occurring zinc finger protein (claim 21 and claims dependent

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therefrom). Applicants also note that the claims have been amended to recite functional domains from plants that are known to be functional transcription modulators in plants. (reply pages 6-7).

The rejection is maintained because the claimed invention is not adequately described. While claim 1 has been amended to make explicit that the claimed modified plant zinc finger protein has a "modified" amino acid sequence as compared to a naturally occurring plant zinc finger protein, the claim does not specify in what way the amino acid sequence of claimed protein has been "modified". Claim 1 does not specify that shortening of the inter-finger spacing is the amino acid sequence modification referred to in line 2 of the claim, such that the claim allows for any type of amino acid sequence modification. Further, modified plant zinc finger proteins wherein the only modification made is the alteration of the amino acid sequence of the recognition region (claim 21) are not adequately described, and modified plant zinc finger proteins wherein one or more of the zinc fingers comprise non-canonical zinc fingers are not adequately described, as the specification describes only a single genus of polynucleotides encoding modified plant zinc finger proteins, said polynucleotides encoding polypeptides comprising a tandem array of three modified canonical zinc fingers, two derived from the *Arabidopsis* zinc finger sequences of SEQ ID NOS: 13 and 14 and one derived from the petunia zinc finger sequence of SEQ ID NO: 12, said tandem array being fused to the transcriptional activation domain, and said zinc finger backbones modified by amino acid substitution, addition and deletion to more closely resemble the SP-1 consensus sequence of SEQ ID NO: 11, resulting in the production of the zinc finger backbones of SEQ ID NOS 17-19, with the amino acid sequences of each of the three zinc fingers further

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modified to cause the zinc fingers to bind to 16 different specific target sequences in the *Arabidopsis* GMT gene, each target sequence consisting of 10 contiguous nucleotides (page 42 and Figure 2).

Claim 10 remains rejected, and claim 31 is rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated polynucleotides encoding the exemplified genus of modified plant zinc finger proteins, does not reasonably provide enablement for isolated polynucleotides encoding modified plant zinc finger proteins wherein one or more of the zinc fingers comprise any unspecified non-canonical zinc finger. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record.

Applicant's arguments filed June 10, 2004, have been fully considered but they are not persuasive.

Applicant maintains that the specification fully enables the pending claims, and that the Examiner's concerns about structure, particularly what modifications are encompassed, have been addressed by the current amendments. Similarly, Applicant maintains that the concerns about functional domains have also been obviated. (reply page 7)

The rejection is maintained because the full scope of the claimed invention is not enabled. The rejected claims continue to be directed to modified plant zinc finger proteins wherein one or more of the zinc fingers comprise any unspecified non-canonical zinc finger. In the instant case the specification does not provide guidance with respect to how

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to alter the structure of the zinc finger backbone of any non-canonical plant zinc finger protein relative to a corresponding established non-canonical zinc finger standard. Absent such guidance one skilled in the art would have to determine by trial and error which non-canonical plant zinc finger to alter, which particular corresponding established non-canonical zinc finger to use as a standard for alterations, and which alterations to make, in order to produce a non-canonical zinc finger which, when part of a modified plant zinc finger protein, will cause the modified plant zinc finger protein to function as desired. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 21, and claims dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 21 is indefinite in the recitation of “the modification” in line 4. There is insufficient antecedent basis for “the modification” in claim 21.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 6-9, 11, 17-19 and 21-30 and 32 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Barbas et al. (US Patent No. 6,140,466, issued October 31, 2000 and filed May 27, 1997).

The claims are drawn to a non-naturally-occurring protein comprising a modified plant zinc finger protein (ZFP), the modified plant ZFP having a modified amino acid sequence as compared to a naturally occurring plant ZFP and comprising a tandem array of a plurality of zinc fingers, wherein one or more of the zinc fingers comprise canonical C2H2 zinc fingers and are derived from two or more plant species, wherein there are between about 5 and 50 amino acids between adjacent zinc fingers of the modified plant ZFP, and further wherein the modified plant zinc finger protein is engineered to bind to a target sequence, and to a polynucleotide encoding said non-naturally-occurring protein.

The claims are also drawn to a non-naturally-occurring protein comprising a modified plant zinc finger protein (ZFP) engineered to bind to a target sequence, the modified plant zinc finger protein comprising a plurality of zinc fingers, wherein one or more of the zinc fingers comprise canonical C2H2 zinc fingers and are derived from two or more plant

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species, each zinc finger comprising an amino acid recognition region which binds to a target subsite of the target sequence, wherein the modification comprises one or more amino acid substitutions in the recognition region of one or more of the zinc fingers of the modified plant ZFP as compared to a naturally occurring plant zinc finger protein, and to a polynucleotide encoding said non-naturally-occurring protein.

Barbas et al. teach a non-naturally-occurring protein comprising a modified zinc finger protein (ZFP), the modified ZFP having a modified amino acid sequence as compared to a naturally occurring ZFP and comprising a tandem array of a plurality of zinc fingers, wherein one or more of the zinc fingers comprise canonical C2H2 zinc fingers, wherein there are 5 amino acids between adjacent zinc fingers of the modified ZFP, and further wherein the modified zinc finger protein is engineered to bind to a target sequence, and a polynucleotide encoding said non-naturally-occurring protein. (columns 89-92). Barbas et al. also teach a non- naturally-occurring protein comprising a modified zinc finger protein (ZFP) engineered to bind to a target sequence, the modified zinc finger protein comprising a plurality of zinc fingers, wherein one or more of the zinc fingers comprise canonical C2H2 zinc fingers, each zinc finger comprising an amino acid recognition region which binds to a target subsite of the target sequence, wherein the modification comprises one or more amino acid substitutions in the recognition region of one or more of the zinc fingers of the modified ZFP as compared to a naturally occurring zinc finger protein, and a polynucleotide encoding said non-naturally-occurring protein (columns 89-92).

While Barbas et al. do not teach that their modified zinc finger protein is a “plant” zinc finger protein or that the zinc fingers of their modified zinc finger protein are

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“derived from two or more plant species”, such limitations do not serve to distinguish the claimed modified zinc finger proteins from the modified zinc finger proteins taught by Barbas et al., because the source of a protein (plant versus nonplant) generally does not distinguish it from other proteins having the same structural characteristics and organization, since all proteins are composed of the same 20 amino acids regardless of their source.

In the instant case there are insufficient structural characteristics set forth in the claims to distinguish the claimed proteins from the proteins taught by Barbas et al. While the specification at pages 1-3 does disclose that naturally occurring plant C2H2 zinc finger proteins do not generally occur in closely spaced tandem arrays as do naturally occurring animal C2H2 zinc finger proteins, the specification also discloses that naturally occurring plant C2H2 zinc finger proteins exhibit other features that are characteristic of C2H2 zinc finger proteins obtained from any source, e.g. a zinc finger domain comprising a conserved sequence of approximately 30 amino acids that contains the invariant cysteines and histidines in the following arrangement: -Cys-(X)₂₋₄- Cys-(X)₁₂-His-(X)₃₋₅-His (page 1; page 36).

The specification at page 7 further discloses that “the modified plant ZFPs are organized in non-plant ZFP structures, for example structures in which individual zinc fingers (e.g., C2H2 fingers) are linked by short linker sequences, or structures that do not contain native plant DNA binding sequences such as inter-zinc finger sequences of a plant zinc finger protein”.

The specification at pages 7-8 also discloses that while “the modified plant ZFPS disclosed herein differ from previously described designed zinc finger protein

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transcription factors in that they are entirely or primarily composed of plant sequences”, these plant sequences are nonetheless “assembled such that the overall structure of the binding region of the modified plant protein is similar to that of a non- plant eukaryotic zinc finger”.

The specification additionally discloses at page 10 that “As used herein, the term “modified plant” zinc finger protein refers to a zinc finger protein comprising plant ZFP sequences organized in a non-plant ZFP structure, for example to eliminate the long stretches of amino acid sequence between zinc fingers found in many naturally-occurring plant ZFPs.”

Accordingly, the limitation “plant” recited in the claims as a source for at least some part of the claimed modified zinc finger proteins does not distinguish the claimed modified zinc finger proteins from the modified zinc finger proteins taught by Barbas et al., since the claimed proteins are “non-naturally-occurring”, may have “a modified amino acid sequence as compared to a naturally occurring plant ZFP”, may comprise “a tandem array of a plurality of zinc fingers” and may have “between about 5 and 50 amino acids between adjacent zinc fingers of the modified plant ZFP”, and since the specification indicates that the claimed proteins do not retain those features that are characteristic of C2H2 zinc finger proteins obtained from plant sources.

See MPEP 2113 citing *In re Thorpe* “[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was

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made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

See MPEP 2113 also citing In re Brown “when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable.” In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

MPEP 2113 additionally states that “Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983)”.

See MPEP 2112.01 citing In re Best “Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established.” In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).

See MPEP 2112.01 further citing In re Brown “When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14 and 33 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Barbas et al. (US Patent No. 6,140,466, issued October 31, 2000 and filed May 27, 1997) in view of Choo et al. (US Patent No. 6,706,470, issued March 16, 2004, filed November 28, 2001, and claiming priority under 35 U.S.C. § 365(c) and 35 U.S.C. § 120 as a continuation of PCT/GB00/02071 filed May 30, 2000).

The claims are drawn to a non-naturally-occurring protein comprising a modified plant zinc finger protein (ZFP), the modified plant ZFP having a modified amino acid sequence as compared to a naturally occurring plant ZFP and comprising a tandem array of a plurality of zinc fingers, wherein there are between about 5 and 50 amino acids between adjacent zinc fingers of the modified plant ZFP, and further wherein the modified plant zinc finger protein is engineered to bind to a target sequence, and to a polynucleotide encoding said non-naturally-occurring protein, including a polynucleotide further encoding a C1 functional domain. The claims are also drawn to a non-naturally-occurring protein comprising a modified plant zinc finger protein (ZFP) engineered to bind to a target sequence, the modified plant zinc finger protein comprising a plurality of zinc fingers, each zinc finger comprising an amino acid recognition region which binds to

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a target subsite of the target sequence, wherein the modification comprises one or more amino acid substitutions in the recognition region of one or more of the zinc fingers of the modified plant ZFP as compared to a naturally occurring plant zinc finger protein, and to a polynucleotide encoding said non-naturally-occurring protein, including a polynucleotide further encoding a C1 functional domain.

The teachings of Barbas et al. are set forth above.

Barbas et al. do not teach a C1 functional domain.

Choo et al. teach the use of a maize C1 transcriptional activation domain for expression of engineered zinc finger proteins in plant cells (column 53 lines 29-55; column 54 line 50 through column 55 line 52).

Given the teachings of Choo et al. that a maize C1 transcriptional activation domain is useful for expression of engineered zinc finger proteins in plant cells, would have been *prima facie* obvious to one skilled in the art at the time the invention was made to make a polynucleotide encoding an engineered zinc finger protein as taught by Barbas et al. that further encodes a C1 functional domain. One skilled in the art would have been motivated to do so in order to express engineered zinc finger protein in plant cells such that the transcription of a target gene would be enhanced. One skilled in the art would have had a reasonable expectation of success given that zinc finger proteins and the maize C1 transcriptional activation domain were both known to function to enhance the transcription of target genes in plants. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

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Remarks

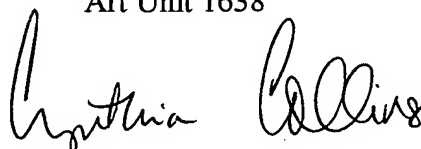
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins
Primary Examiner
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8/21/05

CC